National Center for Emerging and Zoonotic Infectious Diseases

JYNNEOS Vaccine Effectiveness

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Centers for Disease Control and Prevention

Advisory Committee on Immunization Practices

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Background

- **Efficacy** of JYNNEOS against mpox has been **inferred** from animal and immunogenicity studies, but has never been demonstrated in clinical trials
- **No** real-world **vaccine effectiveness** (VE) estimates for JYNNEOS against mpox disease prior to current multinational outbreak
- Key questions:
  1. What is the effectiveness of JYNNEOS vaccine against mpox disease?
     a) What is VE of partial (1 dose) versus full (2 doses) vaccination?
  2. Are there differences in VE by route of vaccine administration?
  3. Are there differences in VE among persons with immunocompromising conditions?
  4. What is the duration of protection conferred from JYNNEOS vaccine?

Organization of presentation

- **Vaccine performance**
  - Incidence of mpox among unvaccinated persons versus persons receiving ≥1 JYNNEOS dose in the United States (U.S)
- **Vaccine effectiveness (VE) of JYNNEOS given as post-exposure prophylaxis (PEP) against mpox disease, New York City**
- **VE of JYNNEOS given as pre-exposure prophylaxis (PrEP) against mpox disease**
  1. **Israel single dose VE Study**: Real-world effectiveness of a single dose of mpox vaccine in males
  2. **EPIC Cosmos Case-Control Study**: VE of 1 and 2 doses against mpox disease in the U.S
  3. **Multi-jurisdictional Case-Control Study**: Interim estimate of VE of 2 doses against mpox disease in 12 U.S. jurisdictions
  4. **New York State Case-Control Study**: Preliminary estimates of VE of 1 and 2 doses against mpox disease

Vaccine performance

Weekly mpox incidence by vaccination status: Methods

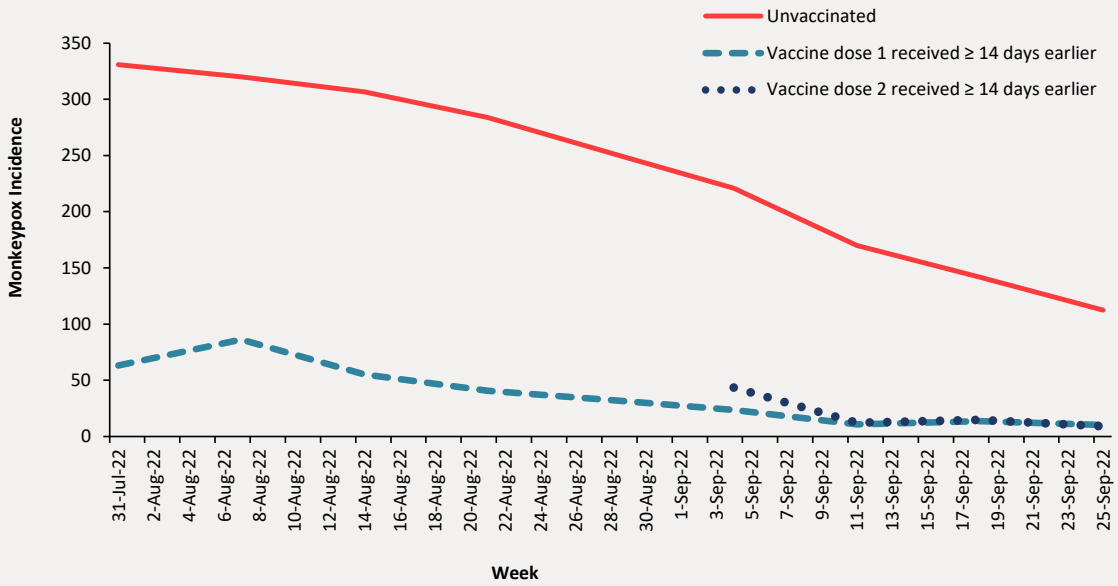
- **Data sources:** Mpox case data, vaccine administration data, estimates of the vaccine eligible population*
- **Design:** Comparison of mpox incidence among persons who were unvaccinated and those who had received either 1 or 2 JYNNEOS doses
- **Population:** 9,544 reported mpox cases among men aged 18–49 years from 43 U.S. jurisdictions
- **Time period:** July 31–October 1, 2022
- **Analysis:**
  - Estimated weekly mpox incidence for persons with partial (1 dose) and full (2 doses) vaccination and persons eligible but unvaccinated
  - Calculated incidence rate ratio using negative binomial regression

*Estimated population per jurisdiction of men who have sex with men (MSM) who are living with HIV or MSM who are eligible for HIV pre-exposure prophylaxis.

Source: Payne AB, et al. Reduced Risk for Mpox After Receipt of 1 or 2 Doses of JYNNEOS Vaccine Compared with Risk Among Unvaccinated Persons — 43 U.S. Jurisdictions, July 31–October 1, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1560–1564.

Weekly mpox incidence,* by vaccination status among males aged 18–49 years eligible for vaccination§

July 31, 2022 – October 1, 2022 (43 U.S. jurisdictions)**



Mpox incidence among unvaccinated individuals was **7.4 (95% CI = 6.0–9.1)** times as high as **persons receiving 1 dose of JYNNEOS vaccine**.

Mpox incidence among unvaccinated individuals was **9.6 (95% CI = 6.9–13.2)** times as high as **persons receiving 2 doses of JYNNEOS vaccine**.

No difference observed in vaccine performance **between subcutaneous and intradermal administration**.

* Cases per 100,000 population. Rate in vaccinated persons = number of probable or confirmed cases reported to CDC with date of illness onset, specimen collection, lab test completion, admission, diagnosis, discharge, case investigation start date, or date first electronically submitted or reported to the county, state, or public health department (earliest available date) ≥14 days after receiving the first dose or second dose of JYNNEOS vaccine among total vaccinated population as of 2 weeks previously. Rate in unvaccinated persons = number of probable or confirmed cases reported to CDC without evidence of vaccination among total unvaccinated population.

§ Gay, bisexual, and other men who have sex with men who have HIV infection or who are eligible to receive HIV preexposure prophylaxis were considered eligible for vaccination.

¶ Alabama, Alaska, California, Colorado, Connecticut, District of Columbia, Florida, Georgia, Hawaii, Idaho, Illinois, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nevada, New Hampshire, New Mexico, New York (excluding New York City), North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Virginia, West Virginia, Wisconsin, and Wyoming.

** Jurisdictions were included if age and sex assigned at birth or gender identity was available for ≥70% of cases reported, vaccination status was available for ≥50% of cases in males (defined by either sex assigned at birth or gender identity) aged 18–49 years or the jurisdiction confirmed cases were linked to immunization registry entries, and de-identified vaccination administration data were submitted to CDC.

Source: Payne AB, et al. Reduced Risk for Mpox After Receipt of 1 or 2 Doses of JYNNEOS Vaccine Compared with Risk Among Unvaccinated Persons — 43 U.S. Jurisdictions, July 31–October 1, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1560–1564.

Vaccine effectiveness of JYNNEOS administered as PEP against mpox

JYNNEOS effectiveness as PEP against mpox, New York City (unpublished data)

- **Design:** Cohort evaluation of individuals ages ≥18 years residing in NYC identified through routine Department of Health contact investigations to a case-patient with mpox between May 22—August 24, 2022 and no vaccination or disease history prior to exposure
- **PEP**: Receipt of 1st dose of JYNNEOS ≤14 days of exposure and prior to date of symptom onset, if applicable
- **Case-patient**: Exposed individuals who developed symptom onset ≤ 21 days after exposure (incubation period) with laboratory confirmation
- **Analysis**: VE of a single dose of JYNNEOS administered subcutaneously ≤14 days after exposure as PEP for preventing laboratory-confirmed mpox disease as [(1 – Relative Risk) × 100%]
- **Results:** Among individuals with high-risk* exposure, **vaccine effectiveness was 77% (95% CI: 51%-92%) with PEP <14 days after last exposure** (n=273) and **79% (46%-94%) with PEP <14 days after first exposure (n=208)****

*Defined according to the CDC Interim Community Exposure Risk Assessment and Recommendations

***Unadjusted; in univariate analyses, race/ethnicity and age-group were not significantly associated with mpox disease

Vaccine effectiveness of JYNNEOS administered as PrEP against mpox

Israel single-dose VE study: Methods

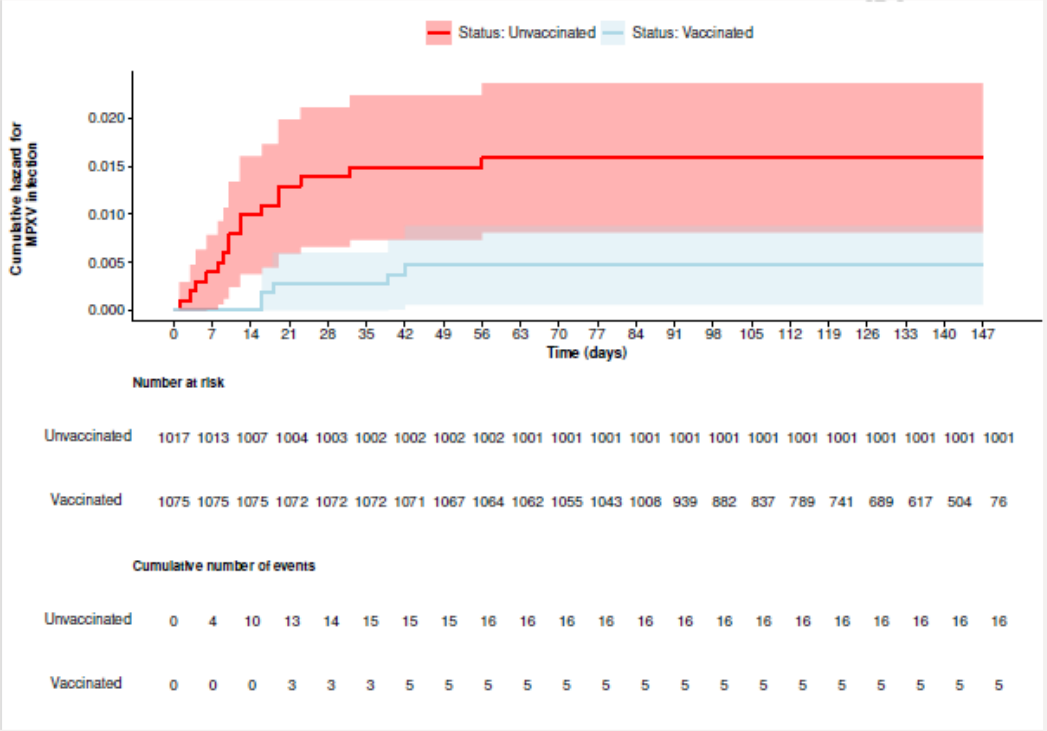
- **Vaccination:** Single, subcutaneous dose of Modified Vaccinia Ankara-Bavarian Nordic (MVA-BN)
- **Design:** Retrospective, observational cohort using electronic health records from a single integrated health center in Israel
- **Population:** 2,054 men eligible* for vaccination
- **Time period:** July 31, 2022 – December 25, 2022
- **Analysis:**
  - **VE estimated** using Cox proportional hazards regression with vaccination status as a time-varying covariate
  - Model **adjusted for** sociodemographic and clinical risk factors

*Males aged 18 – 42 years who were dispensed HIV-PrEP at least for one month since January 1, 2022, or (b) males aged 18 – 42 years who were diagnosed with HIV and also were diagnosed with one or more sexually transmitted infections (STIs) since January 1, 2022.

Source: Sagy, Y. W. et al. Real-world effectiveness of a single dose of mpox vaccine in males. Nature Medicine https://doi.org/10.1038/s41591-023-02229-3 (2023).

Israel single-dose VE study: Results

- **5 mpox cases** among **vaccinated individuals**
- **16 mpox cases** among **unvaccinated individuals**
- Adjusted single-dose vaccine effectiveness was 86% (95% CI: 59%-95%)



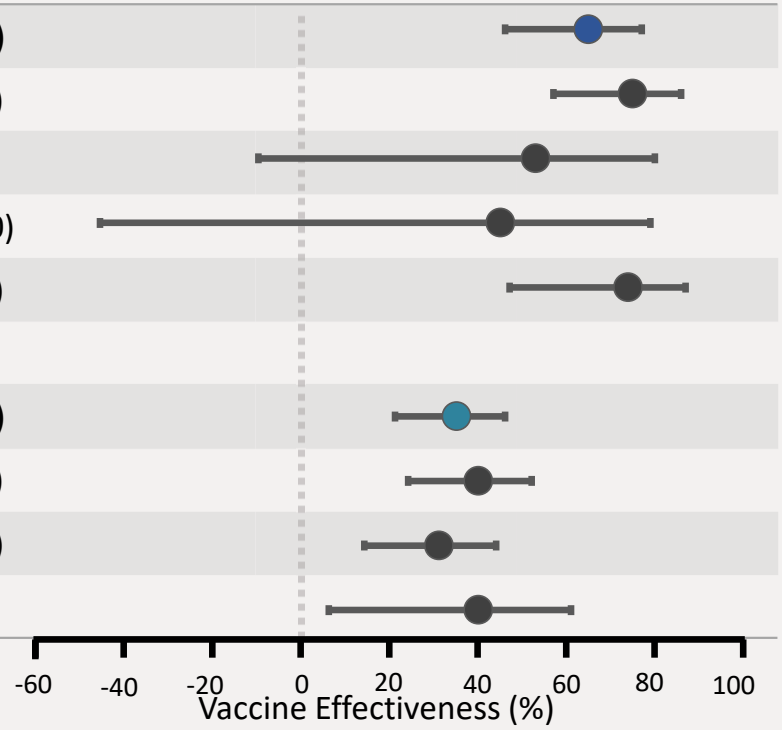
Source: Sagy, Y. W. et al. Real-world effectiveness of a single dose of mpox vaccine in males. Nature Medicine https://doi.org/10.1038/s41591-023-02229-3 (2023).

Epic Cosmos Case-Control Study: Methods

- **Data Source:** Epic's electronic health record (EHR) platform, Cosmos, which includes records from >169 million patients across the U.S.
- **Design:** Case-control analysis, matched 1:4 based on week of index event, HHS region, and gender identity
  - **Case patients**: Patients with an mpox diagnosis or positive orthopoxvirus or mpox virus laboratory result from 8/15 - 11/19/2022
  - **Control patients**: Patients with an incident HIV diagnosis or HIV pre-exposure prophylaxis (PrEP) prescription from 8/15 - 11/19/2022
- **Analysis:**
  - **VE estimated** using conditional logistic regression
  - **Adjusted for** age, race/ethnicity, social vulnerability index, immunocompromising conditions
  - **Stratified by** route of administration and immunocompromised status

Epic Cosmos Case-Control Study: JYNNEOS VE for full and partial vaccination, August 15-November 19, 2022, United States (unpublished data)

	Cases (n=2,913)	Controls (n=8,319)	Adjusted* VE (95% CI)
Overall VE, full vaccination (2 doses)	**25**	**335**	**66 (47, 78)**
No immunocompromising conditions	14	312	76 (58, 87)
2 doses administered subcutaneously	6	63	54 (-9, 81)
2 doses administered intradermally	5	42	46 (-45, 80)
2 doses administered heterologously	8	150	75 (48, 88)
Overall VE, partial vaccination (1 dose)	**146**	**1000**	**36 (22, 47)**
No immunocompromising conditions	102	932	41 (25, 53)
1 dose administered subcutaneously	106	704	32 (15, 45)
1 dose administered intradermally	27	186	41 (7, 62)



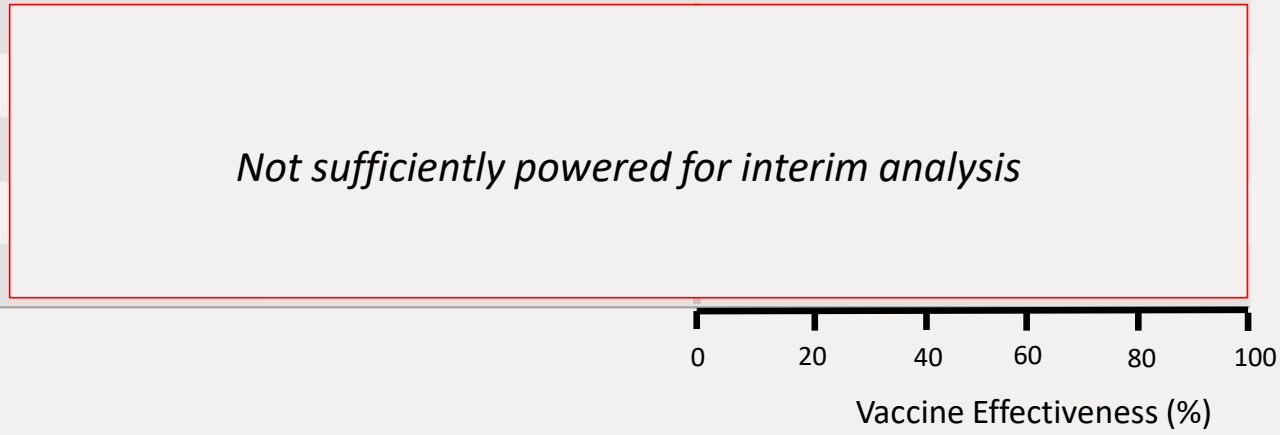
*Adjusted for age, race/ethnicity, social vulnerability index, and immunocompromising conditions.
Cases/controls matched on week of index event, HHS region, gender identity.

Multi-jurisdictional Case-Control Study: Methods

- **Design:** Case-control study
- **Population:** Men who have sex with men; ages 18-49; 12 U.S. jurisdictions
- **Methods:**
  - **Cases** identified from jurisdictions' probable and confirmed mpox case lists
  - **Controls** identified from healthcare settings providing HIV PrEP or sexually transmitted infection (STI) clinics
  - Demographics, exposure history, and vaccination history collected using electronic surveys
  - Vaccination status confirmed by state immunization registries
- **Analysis:** Logistic regression with random intercept for jurisdiction and adjusted for age, race/ethnicity, number of sexual partners, close contact with a confirmed/probable case, and month of index event

Multi-jurisdictional Case-Control Study Interim Results: VE for full vaccination (unpublished data)

	Cases (n=167)	Controls (n=256)	Adjusted* VE (95% CI)
Overall VE, full vaccination (2 doses)	**14**	**122**	76% (48%-89%)
No immunocompromising conditions	8	61	90% (66%-97%)
Immunocompromising conditions			
Overall VE, partial vaccination (1 dose)			
No immunocompromising conditions			
Immunocompromising conditions			



*Adjusted for age, race/ethnicity, immunocompromised status, reported close contact with a confirmed/suspected mpox case in 3 weeks prior to index event, and month of index event

New York State Case-Control Study: Preliminary Estimates (unpublished data)

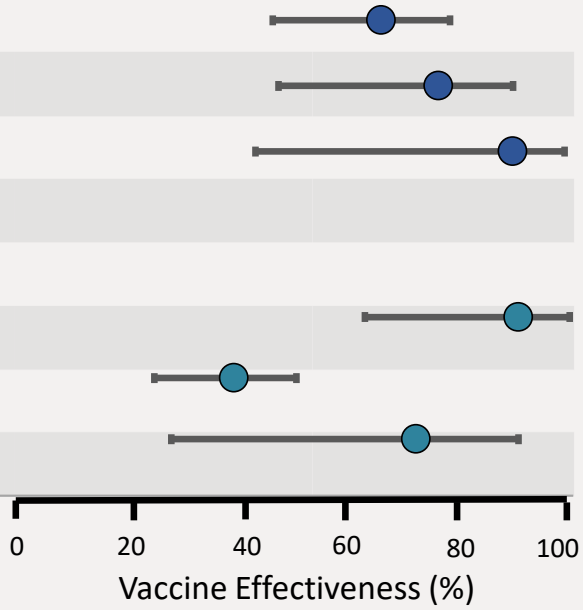
- **Data source:** Linkage of case surveillance to immunization registry in New York State, excluding New York City
- **Cases**: Adult male mpox cases during July 24 – October 31, 2022
- **Controls**: Adult male STI cases (rectal gonorrhea or primary syphilis) during July 24 – October 31, 2022
- **Analysis:** Conditional logistic regression model adjusted for diagnosis week, race, age, region within state

	mpox cases (n=252)	STI controls (n=255)	VE (95% CI)
Unvaccinated	230 (91%)	204 (80%)	*ref.*
Partial vaccination	10 (4%)	23 (9%)	**68% (25%, 86%)**
Full vaccination	2 (1%)	19 (7%)	**89% (44%, 98%)**

Summary

Vaccine effectiveness of JYNNEOS against mpox ranges from 66%-89% for full vaccination and 36%-86% for partial vaccination

	Cases	Controls	Adjusted* VE (95% CI)
Full vaccination (2 doses)			
Epic Cosmos case-control study	25	335	66% (47%- 78%)
Multi-jurisdictional case-control study	14	122	76% (48%-89%)
New York State case-control study	2	19	89% (44%-98%)
Partial vaccination (1 dose)			
Israel single-dose study	5	16	86% (59%-95%)
Epic Cosmos case-control study	146	1000	36% (22%-47%)
New York State case-control study	10	23	68% (25%-86%)



Vaccine effectiveness of JYNNEOS against mpox

- JYNNEOS vaccine is effective at reducing risk of mpox disease
- Protection provided by both 1 and 2 doses of JYNNEOS vaccine
- Highest protection provided by 2 doses, regardless of route of administration
- Further research needed to evaluate whether immunocompromised status modulates VE
- Further research needed to assess duration of protection

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